ACUCELA

Press Release

Acucela Initiates Phase 3 Study of Emixustat Addressing Patients with Stargardt Disease

SEATTLE (November 11, 2018) — Acucela Inc. ("Acucela"), a clinical-stage ophthalmology company and wholly-owned subsidiary of Kubota Pharmaceutical Holdings Co., Ltd. (Tokyo 4596), announced today that on November 7, 2018, the first patient has enrolled (FPFV; first patient first visit) in a study to evaluate Acucela's leading drug candidate, emixustat hydrochloride ("emixustat"), in subjects with macular atrophy secondary to Stargardt disease.

The study is a multi-center, randomized, double-masked, and placebo-controlled phase 3 clinical study in which subjects will be randomly assigned to emixustat 10 mg or placebo (2:1 ratio) once daily for 24 months. Approximately 160 subjects will be enrolled at 30 sites in 10 countries worldwide.

The primary objective of this study is to determine if emixustat reduces the rate of macular atrophy progression, in comparison to placebo, in subjects with Stargardt disease. Secondary objectives include assessing changes in visual function parameters such as BCVA (best-corrected visual acuity) letter score and reading speed.

Dr. Ryo Kubota, MD, PhD, and Chairman, President and CEO of Acucela stated that "We are very excited to be proceeding with the phase 3 clinical study addressing Stargardt disease with emixustat. Stargardt is an unmet medical need with no known therapies to slow the progression of the disease. We are now focused on initiating our study to advance our clinical program, to help patients facing vision loss and blindness from this disease."

The FDA (U.S. Food and Drug Administration) granted orphan drug designation to emixustat for the treatment of Stargardt disease. (See January 5, 2017 press release titled "Acucela Receives Orphan Drug Designation from the FDA for the Treatment of Stargardt Disease")

About Stargardt Disease

Stargardt disease, or fundus flavimaculatus, is a rare, genetically inherited disease that directly affects the retina of the eye, often resulting in the slow progression of vision loss in children. It may also be referred to as Stargardt macular dystrophy or juvenile macular degeneration and affects approximately 1 in 8,000 - 10,000 individuals worldwide [(1)]. The most common form of the disease is caused by a genetic mutation of the ABCA4 gene leading to the accumulation of toxic vitamin A byproducts (primarily A2E) in the retina, which results in the gradual deterioration of photoreceptors and vision. Symptoms of Stargardt disease typically appear during childhood or adolescence, but in some cases difficulty with eyesight and vision loss may not be identified until later in life.

Stargardt disease affects less than 40,000 patients in the U.S. where it is recognized as an orphan disease, subject to the Orphan Drug Act. Currently, there are no known therapies that exist to slow the advance of the disease, and it is recognized as a serious unmet medical need by the United States Foundation of Fighting Blindness and the National Eye Institute.

(1) Facts About Stargardt Disease, National Eye Institute. https://nei.nih.gov/health/stargardt/star_facts, accessed on 14 September 2018.

About Emixustat Hydrochloride

The visual cycle is the process by which vitamin A is recycled in the eye; vitamin A is crucial to the visual process. Emixustat modulates the visual cycle by inhibiting a critical enzyme of this pathway, retinal pigment epithelium protein 65 (RPE65). Slowing the visual cycle reduces the availability of vitamin A derivatives (11-cis- and all-trans-retinal) to form precursors of A2E and related compounds. In animal models of Stargardt disease and retinal degeneration, emixustat was found to stop and reverse the accumulation of A2E and to preserve the integrity of the retina. Emixustat when delivered orally was found to be generally well tolerated in human clinical studies with delayed dark adaptation being the most common ocular adverse event.

About Acucela Inc.

Acucela Inc. is a wholly-owned subsidiary of Kubota Pharmaceutical Holdings Co., Ltd. (Tokyo 4596) committed to translating innovation into a diverse portfolio of drugs and devices to preserve and restore vision for millions of people worldwide. Acucela's development pipeline include drug candidates for the treatment of diabetic retinopathy, diabetic macular edema, Stargardt disease, age-related macular degeneration, cataracts and presbyopia, and, optogenetics-based gene therapy for the treatment of retinitis pigmentosa. The company is also developing a handheld OCT device for the monitoring of neovascular retinal diseases, to be used directly by patients. http://www.acucela.com; http://www.kubotaholdings.co.jp/en/

Cautionary Statements

Certain statements contained in this press release are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995. Any statements contained in this press release that are not statements of historical fact may be deemed to be forward-looking statements. These forward-looking statements include statements regarding our expectations related to our development plans and ability to successfully develop and commercialize our product candidates and the potential efficacy, future development plans and commercial potential of our product candidates. These statements are based on current assumptions that involve risks, uncertainties and other

factors that could cause the actual results, events or developments to differ materially from those expressed or implied by such forward-looking statements. These risks and uncertainties, many of which are beyond our control, include, but are not limited to: our investigational product candidates may not demonstrate the expected safety and efficacy; our pre-clinical development efforts may not yield additional product candidates; any of our or our collaborators' product candidates may fail in development, may not receive required regulatory approvals, or may be delayed to a point where they are not commercially viable; our clinical trials could be delayed; new developments in the intensely competitive ophthalmic pharmaceutical market may require changes in our clinical trial plans or limit the potential benefits of our investigational product candidates; the impact of expanded product development and clinical activities on operating expenses; adverse conditions in the general domestic and global economic markets; as well as the other risks identified in our filings with the Securities and Exchange Commission. These forward-looking statements speak only as of the date hereof and we assume no obligation to update these forward-looking statements, and readers are cautioned not to place undue reliance on such forward-looking statements. For a detailed discussion of the foregoing risks and other risk factors, please refer to our filings with the Securities and Exchange Commission, which are available on Kubota Pharmaceutical Holdings (Acucela's parent company) investor relations website (http://www.kubotaholdings.co.jp/en/ir/) and on the SEC's website (http://www.sec.gov).

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